# PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
PAMELA J. SHERWOOD
BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVENUE, SUITE 200
EAST PALO ALTO, CA 94303

REC'D 2 AUG 2005
PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

| | |
|---|---|
| Applicant' s or agent's file reference<br>SEEK-006WO | Date of mailing (*day/month/year*) 18 AUG 2005<br>FOR FURTHER ACTION<br>See paragraph 2 below |

| International application No. | International filing date (*day/month/year*) | Priority date (*day/month/year*) |
|---|---|---|
| PCT/US04/12449 | 23 April 2004 (23.04.2004) | 23 April 2004 (23.04.2004) |

International Patent Classification (IPC) or both national classification and IPC

IPC(7): GO 1N 33/48, GO 1N 33/53 and US Cl.: 702/19, 435/7.1

Applicant

IVAN PLAVEC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| | |
|---|---|
| Name and mailing address of the ISA/ US<br>Mail Stop PCT, Attn: ISA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (703) 305-3230 | Authorized officer<br>Marjorie Moran<br>Telephone No. (571)272-0720 |

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/12449

**Box No. I Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language ____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/12449

**Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | |
|---|---|---|
| Novelty (N) | Claims NONE | YES |
| | Claims 1-10 | NO |
| Inventive step (IS) | Claims NONE | YES |
| | Claims 1-10 | NO |
| Industrial applicability (IA) | Claims 1-10 | YES |
| | Claims NONE | NO |

2. Citations and explanations:

Claims 1-10 lack novelty under PCT Article 33(2) as being anticipated by Berg et al, WO 01/067103.

Berg discloses a method for determining components of a signaling pathway (see generally legends for Fig. 16, p. 11 and Fig. 17, p. 12. Berg discloses both not genetically altered cells and cells that have been transfected or transducted with recombinant genes or the antisense technology (p. 20). The method comprises a step of exposing a set of recombinant cells to at least one factor that activates or inhibits the pathway (see Examples 10-11 wherein HUVEC cells are transfected with recombinant vectors comprising members Bcl-3 and Bcl-xL that overexpressed in the cells and are the members of a signaling pathway, p. 78-80).. The method further comprises a step of recording changes in at least two different cellular parameter readouts after exposure (ICAM-1, VCAM-1 and MIG, page 80). The method also comprises a step of deriving a functional profile (a biomap; *see* for the biomap description p. 15-17) from the changes of the parameter readout (p. 79, line 21 and p. 80, line 22). The method may comprises a step of clustering as described in " Data Analysis" section on p. 41-43 and a legend to Fig. 2, p. 6 and Fig. 4C, p. 7. Thus, Berg anticipates claim 1.

Berg discloses a method for determining the presence of an interaction between a first and a second signaling pathway. The method comprises steps of exposing recombinant cells to activating/inhibiting factors, recording changes in at least two cellular parameters, deriving a functional profile from the changes of the parameters, and determining one gene in one pathway responds similarly to the response by another gene in another pathway (see Example 11, p. 79-80). Thus, Berg anticipates claim 2.

Berg discloses a method of ordering the components of a signaling pathway comprising steps of exposing cells to a first inhibitor of a signaling pathway, exposing cells to a second inhibitor of the pathway, recording changes in at least two different parameters, and determining relationship between components and inhibitors of the pathway (*see* examples on p. 60 and p. 80). Thus, Berg anticipates claim 3.

Berg discloses a method of determining a mechanism of action for a test compound on a signaling pathway comprising steps of exposing recombinant cells to a test compound, recording changes in at least two cellular parameters after the exposure, deriving a functional profile, comparing the profile with that of a control compound, and determining comparable functional profile of the test compound (*see* for all steps examples on p. 64-65, table 1 on p. 66-67 and text on p. 67; see also Figs. 4A-C illustrating the method). Berg states that the example on p. 64-67 demonstrates that the biomaps (functional profiles) are useful in distinguishing the mode of action of candidate compounds, so as to know whether combinations of compounds act on the same or different pathway (p. 68). Thus, Berg anticipates claim 4. Berg discloses a factor that activates or inhibits a signaling pathway (see, for example, p. 61, line24-25), thus anticipating claim 5. Berg discloses undeexpression of a target gene as a result of exposure to an agent (see Fig. 2B), thus anticipating claims 6-8. Berg discloses detection of at least four cell parameters (see, for example, p. 59, line 17-18), thus anticipating claim 9. Berg discloses ordering of functional plots (biomaps) in graphs wherein graphs comprise annotations (see p. 16). It is known that annotated graphics (plots) represent two dimensional scaling plots. Also, Berg discloses cluster plots (see fig. 2 and 4), thus Berg anticipates claim 10.

Claims 1-10 meet the criteria set out in Article 33(4), and have industrial applicability because the subject claimed can be made or used in industry for data generation related to different disorders and identification of compounds for treating disorders.